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Routine or on Demand Radiological Contrast Examination in the Diagnosis of Anastomotic Leakage After Esophagectomy

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Background: To detect anastomotic leakage after esophagectomy in esophageal carcinoma patients, many surgeons perform a radiological contrast examination routinely. The aim of this retrospective study is to determine the clinical relevance of a routine contrast examination after esophagectomy and to evaluate criteria for contrast examination on demand.

Methods: Data were obtained from 211 patients with cancer of the esophagus or gastro-esophageal junction who underwent an esophagectomy during the period 1991–2004. Retrospectively, we analyzed patients regarding anastomosis-related characteristics and clinical signs including sepsis, fever $\geq$39.0°C, leukocytosis $\geq 20 \times 10^9$/ml and pleural effusion.

Results: Anastomotic leakage had appeared in 35 of the 211 patients. The clinical signs sepsis (odds ratio (OR) 6.72: 95% confidence interval (CI) (2.57–17.56); $P < 0.0001$), leukocytosis (OR 2.62 (1.10–6.22); $P < 0.030$), and fever (OR 2.34 (1.01–5.42); $P < 0.047$) were significantly related to anastomotic leakage. Pleural effusion was not significantly related to anastomotic leakage (OR 2.83 (0.98–8.13); $P = 0.054$).

Conclusion: Our study suggests that the clinical value for a routinely performed contrast examination is debatable. We recommend performing a contrast examination based on clinical suspicion and clinical signs of anastomotic leakage including sepsis, fever $\geq$39.0°C and leukocytosis $\geq 20 \times 10^9$/ml.

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KEY WORDS: esophageal cancer; esophagectomy; anastomotic leakage; contrast examination

INTRODUCTION

Anastomotic leakage is one of the most serious complications after esophagectomy in patients with esophageal carcinoma. The incidence is between 5% and 20% and the subsequent mortality rates range from 12% to 50% [1–4]. Many surgeons apply for a routine radiological contrast examination to detect anastomotic leakage early in the postoperative period. The clinical relevance of this routine examination is debatable. Some authors recommend routine radiological contrast examination to detect an asymptomatic, so called sub-clinical or silent leak, before the start of oral intake [5,6]. On the other hand, several previous studies have shown that its sensitivity is relatively low and they suggest radiological imaging only in case of clinical signs [7–9]. Moreover, in case of a silent leak, resumption of oral food intake usually will not lead to clinical signs [8,9]. However, it is still uncertain if contrast radiological examination could be omitted in the absence of clinical signs of anastomotic leakage.

The aim of this study is to determine the clinical relevance of a routine radiological contrast examination after esophagectomy and to evaluate criteria for a radiological contrast examination on demand. Therefore, we retrospectively analyzed the occurrence of anastomotic leakage in patients who underwent an esophagectomy in our hospital with respect to the presence or absence of clinical symptoms, including sepsis, fever, leukocytosis, and pleural effusion.

METHODS

Patients

The study population consisted of 211 patients with cancer of the esophagus or gastro-esophageal junction who had a curative intended resection in the period 1991–2004. From the date of surgery until the study end, relevant clinical and pathological data and follow-up information was obtained from all medical records and a medical database. Missing information was collected from general practitioners and the Comprehensive Cancer Center North Netherlands. These data included patient demographics, tumor characteristics, treatment related factors, and postoperative course (morbidity, mortality, and hospital course). Postoperative mortality was defined as in-hospital death or death within 30 days. Survival was defined as overall death after the operation. Data were analyzed retrospectively. The study population consisted of 168 (79%) males and 43 (21%) females with a median age of 63.5 years (range 29–83; Table I).

Surgical Management

A curatively intended radical esophagectomy with a two-field lymphadenectomy was performed in all patients with invasive esophageal cancer. Resection was carried out through a left-sided thoracolaparotomy in 114 patients (54.0%), through a right-sided thoracolaparotomy in 94 patients (44.5%) and 3 patients with in-situ cancer underwent a transhiatal procedure (1.4%). A cervical anastomosis was performed in 77 cases (Table II).

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TABLE I. Patients' and Tumor Characteristics

Characteristic	N (%)
Gender	
Male	168 (79.6)
female	43 (20.4)
Age	
Median (years)	63.5 (range 29–83)
Type of resection	
Thoracolaparotomy left	114 (54.0)
Thoracolaparotomy right	94 (44.5)
Transhiatal	3 (1.4)
Histology	
Adenocarcinoma	172 (81.5)
Squamous cell carcinoma	28 (13.3)
Others	11 (5.2)
Localization	
High/mid	15 (7.1)
Distal	112 (53.1)
Gastro-esophageal junction	84 (39.8)
Tumor stage	
I	33 (15.7)
IIa	55 (26.1)
IIb	24 (11.4)
III	84 (39.8)
IVa	15 (7.1)

Resection was not performed when distant metastatic disease was found at laparotomy or in case of extensive nodal involvement within 1 cm from the celiac trunk. Reconstruction was performed by creating a gastric tube vascularized on the right gastric and the right gastroepiploic arteries. A hiatal phrenotomy allowed the passage of at least four fingers to prevent vascular compromise of the substitute. The gastric tubes were positioned in the posterior mediastinum and all anastomoses were performed manually in one-layer. Oral intake of clear water was permitted within the first postoperative days, followed by liquid food from day 5 on. Usually free solid food intake was initiated from day 7 on. Management of anastomotic leakage was either conservative, including drainage with supportive care or by surgical reexploration with adequate drainage. Patient who received primary conservative treatment but underwent surgical reexploration when improvement hold off, were recorded as having both conservative and surgical treatment.

TABLE II. Anastomosis-Related Characteristics

Characteristic	N (%)
Anastomotic leakage	35 (16.6)
Site anastomosis	
Cervical	77 (36.5)
Intrathoracic	134 (63.5)
Incidence of leakage	
Cervical anastomosis	10 (13.0)
Intrathoracic anastomosis	25 (18.7)
Time of leakage (days)	
median	7.0 (range 1–37)
Treatment	
Conservative	20 (57.1)
Surgical	8 (22.9)
Both	7 (20.0)
Contrast examination	
Water-soluble	22 (48.9)
CT oral contrast	22 (48.9)
Chest X-ray	1 (2.2)

Diagnosis of Anastomotic Leakage

During the study period, anastomotic leakage was established in different manners. Generally, the indication for a radiological contrast examination was determined by the responsible surgeon. It was usually based on clinical suspicion and on the surgeon's physical examination. Occasionally, a radiological contrast examination was performed without apparent clinical suspicion as a routine procedure to warrant that the patient had no anastomotic leakage. The radiological procedure consisted of either a water-soluble contrast X-ray examination or a water-soluble contrast computed tomographic examination (CT). In some cases an anastomotic leakage was already suspected on routine chest X-ray procedure. Anastomotic leakage was defined as the occurrence of extraluminal contrast on a radiological examination or signs of unexplained pneumomediastinum or pneumothorax. These signs of leakage on a chest X-ray were considered as proof of leakage as it had the same clinical value and led to the same treatment approach as a regular contrast examination. In some patients leakage was identified by oral methylene blue examination or the occurrence of a high concentration of amylase in the thoracic drainage fluid before radiological examination. These suspected cases were considered as having an anastomotic leakage. Patients with an urgent reoperation for clinically proven anastomotic dehiscence were also recorded. We recorded the occurrence of anastomotic leakage, location of the anastomosis, the presence of clinical signs of leakage, the reason to perform a radiological examination, time in days between primary surgery and leakage, type of contrast examination and treatment of leakage.

Clinical Symptoms

We recorded four relevant clinical signs to predict anastomotic leakage, including the signs of systemic inflammatory response syndrome (SIRS), leukocytosis, defined as a leukocyte count $\geq 20 \times 10^9$/ml, fever defined as temperature $\geq 39.0^{\circ}$C, pleural effusion, defined as increased pleural fluid postoperatively, and sepsis [10]. Because leukocytosis (leukocyte count $>10 \times 10^9$/ml) and a rise in temperature commonly appear after major surgery, a leukocyte count $\geq 20 \times 10^9$/ml and a temperature $\geq 39.0^{\circ}$C were taken as the cut-off points [11]. Due to missing data of 12 patients, none with anastomotic leakage, the clinical signs could be analyzed in 199 patients. Leukocytosis and fever were scored in patients with clinical suspicion at the time of clinical presentation of a suspect anastomotic leakage or at the time of contrast examination. In patients with no clinical suspicion, the highest leukocyte count after operation was recorded. Sepsis was defined as the presence of a systemic inflammatory response and a proven infection by pathogenic or potentially pathogenic micro-organisms [12].

Statistical Analysis

For the analysis of the influence of sepsis, fever, leukocytosis, and pleural effusion on the occurrence of anastomotic leakage we used univariate and multivariate logistic regression. Multivariate logistic regression was performed by incorporating factors as covariates with a P-value ≤ 0.1 on univariate logistic regression analysis. Association between these four factors was analyzed using a Chi-square test. The prognostic impact of anastomotic leakage on postoperative mortality and survival was determined by the Kaplan–Meier method and the log rank test was used for comparison between the curves. A P-value of <0.05 was considered to be significant. Interval was given in median and range. Statistical analyses were all performed by using the statistical package SPSS version 16.0 (SPSS, Inc., Chicago, IL).

RESULTS

General

Anastomotic leakage appeared in 35 of 211 patients (16.6%) with a median time of 7 days after resection (range 1–37 days; Table II). Most patients with an anastomotic leakage had an intrathoracic anastomosis (n = 25/35; 63.5%), but the site of the anastomosis had no significant influence on its occurrence ($P < 0.286$). Of the 45 patients who underwent a radiological examination of the anastomotic site, a water-soluble examination was performed in 22 patients and another 22 patients underwent a CT with oral contrast examination and 1 patient underwent a chest X-ray. Aspiration pneumonia occurred one (2.2%) of the 44 patients after oral contrast examination. The oral intake was recorded in 26 of the 35 patients with anastomotic leakage. Most (n = 21/26, 80.7%) received oral feeding after the disclosure of an anastomotic leak. Re-thoracotomy was performed in seven patients (7/35; 20%), all within 8 days after surgery, due to severe clinical signs of the patients. Overall survival including postoperative mortality showed a significant difference between patients with anastomotic leakage and those without anastomotic leakage (mean 67.2 vs. 41.3 months, respectively, $P < 0.009$). For patients who survived beyond 30 days after surgery, no significant difference in survival related to anastomotic leakage was observed (mean 71.7 vs. 51.9 months, respectively, $P = 0.108$).

Anastomosis-Related Factors

The four signs sepsis, fever, leucocytosis, and pleural effusion were analyzed in 199 patients to determine whether they were significantly related to anastomotic leakage. The overall occurrences of these potential factors were 12.6% (25/199), 29.6% (59/199), 26.1% (52/199), and 8.5% (17/199) for sepsis, fever, leukocytosis, and pleural effusion, respectively. As can be seen in Table III, in the univariate analysis sepsis, fever and leukocytosis were significantly related to anastomotic leakage. Pleural effusion was not significantly related to anastomotic leakage (odds ratio (OR) 2.83: 95% confidence interval (CI) 0.98–8.13; $P < 0.054$). Logistic regression was used to determine which signs were significantly independent prognostic factors of anastomotic leakage (Table III). Sepsis (OR 6.72; 95% CI 2.57–17.56; $P < 0.000$), leukocytosis (OR 2.62; 95% CI 1.10–6.22; $P < 0.030$) and fever (OR 2.34; 95% CI 1.01–5.42; $P < 0.047$) were significantly related to anastomotic leakage. Further analysis of the clinical signs revealed that all signs (sepsis, fever, leukocytosis, and pleural effusion) were significantly related to each other, except for leukocytosis and pleural effusion.

DISCUSSION

The clinical relevance of a routinely performed contrast examination is debatable after esophagectomy when there are no clinical signs of leakage. A radiological contrast examination should be performed on demand when there is clinical suspicion based on clinical signs. In this study sepsis, fever, and leukocytosis showed to be relevant clinical signs of anastomotic leakage. Pleural effusion alone was not related to anastomotic leakage. This article is one of the first reporting the clinical signs of an anastomotic leak that could be defined after esophagectomy. Previous studies regarding the effectiveness of a contrast examination suggested there is no role for a routine oral contrast examination since the sensitivity is low [7,9,13]. Other authors support the use of a routinely performed contrast examination, despite its low sensitivity, because of the risk of severe clinical deterioration in patients with a sub-clinical leak after initiation of oral intake [5,6]. Tirnaksiz et al. [9] found that radiologically detected leaks without clinical signs could remained asymptomatic even after reintroduction of oral feeding. They concluded that a water-soluble contrast examination should be used only when there is clinical suspicion of clinical leakage. Lamb et al. [8] investigated the role of a contrast examination after total gastrectomy emphasizing the value of clinical suspicion in assessing the use of a contrast examination.

Radiological contrast examination may be helpful to access stricture and gastric emptying. However, on a routine basis it seems to be unnecessary to detect anastomotic leakage in many patients. In our study there were nine patients who had a routine contrast examination. However, 170 of the 211 patients (81%) had no clinical suspicion of leakage and did not developed an anastomotic leakage. These patients would have had an unnecessary contrast examination if it was performed on a routine basis. In case of a clear suspicion of anastomotic leakage, patients already underwent a contrast examination or already had a re-thoracotomy for severe mediastinal contamination. These re-thoracotomies were all performed within 8 days after esophagectomy. Since a routine contrast examination is usually performed at day 7 after the operation, these leakages would not have been detected earlier. So, a routine radiological contrast examination could not have prevented this complication. Therefore, we recommend a radiological contrast examination if there are clinical signs of anastomotic leakage such as sepsis, fever, and leukocytosis and not on a routine basis.

Water-soluble contrast examination used to be the standard examination for detecting anastomotic leaks after esophagectomy, but nowadays CT examinations are common. The advantage of CT is the use of both oral and intravenous contrast detecting abscess formation as well. Regarding the superiority of these exams no consensus has been reached. The study of Hogan et al. [14] showed a

TABLE III. Clinical Signs Related to Anastomotic Leakage

	Univariate analysis	95% Confidence interval		
Clinical symptoms	Odds ratio	Lower	Upper	*P*-value
Sepsis	10.00	4.02	24.87	0.000
Leukocytosis	3.28	1.53	7.00	0.002
Fever	3.68	1.73	7.83	0.001
Pleural effusion	2.83	0.98	8.13	0.054
	Logistic regression	95% Confidence interval		
Clinical symptoms	Odds ratio	Lower	Upper	*P*-value
Sepsis	6.72	2.57	17.56	0.000
Leukocytosis	2.62	1.10	6.22	0.030
Fever	2.34	1.01	5.42	0.047

higher specificity for CT compared to water-soluble contrast examination, but in the study of Upponi et al. [15] the specificity was lower while the sensitivity was higher for CT. However, CT is preferred by patients and is more suitable in less mobile patients [14,15]. Other investigators recommend the use of both contrast swallow and endoscopy to confirm a leak in case of clinical suspicion [16]. However, one should be cautious with performing endoscopy in the early postoperative period as the strength of the anastomosis is fragile.

In our study the median time of occurrence of anastomotic leakage was 7 days after surgery, which is comparable with other studies [13]. Since oral feeding in a silent leak does not lead to any clinical signs, solid oral feeding could start after 7 days. Furthermore, it is our policy that patients may drink a small amount of water as early as possible. Oral fluid restriction is not sensible because most patients already swallow their saliva with a daily production of around 1 L [17].

Although we found clinical symptoms related to the occurrence of an anastomotic leak in a large cohort of patients, we acknowledge that there are limitations regarding the number of patients who underwent a routine contrast examination. As this number is low it is impossible to discuss whether a routine contrast examination could detect small or early anastomotic leakage before the appearance of clinical symptoms. It would be interesting to investigate if these anastomotic leakages are severe enough to give clinical deterioration or could stay silent leaks.

In conclusion, the present data did not support a routine use of contrast examination. Since urgent leaks appear earlier and most anastomotic leakages can be detected on time when the examination is based on clinical suspicion. Clinical suspicion can be affirmed by the presence of sepsis, fever $\geq 39.0^{\circ}C$ and leukocytosis $\geq 20 \times 10^9$/ml.

REFERENCES

1. Bartels H, Siewert JR: Therapy of mediastinitis in patients with esophageal cancer. Chirurg 2008;79:30–37.
2. Bonenkamp JJ, Songun I, Hermans J, et al.: Randomised comparison of morbidity after D1 and D2 dissection for gastric cancer in 996 Dutch patients. Lancet 1995;345:745–748.
3. Holscher AH, Vallbohmer D, Brabender J: The prevention and management of perioperative complications. Best Pract Res Clin Gastroenterol 2006;20:907–923.
4. Singh D, Maley RH, Santucci T, et al.: Experience and technique of stapled mechanical cervical esophagogastric anastomosis. Ann Thorac Surg 2001;71:419–424.
5. Sarela AI, Tolan DJ, Harris K, et al.: Anastomotic leakage after esophagectomy for cancer: A mortality-free experience. J Am Coll Surg 2008;206:516–523.
6. Sauvanet A, Baltar J, Le Mee J, et al.: Diagnosis and conservative management of intrathoracic leakage after oesophagectomy. Br J Surg 1998;85:1446–1449.
7. Boone J, Rinkes IB, van Leeuwen M, et al.: Diagnostic value of routine aqueous contrast swallow examination after oesophagectomy for detecting leakage of the cervical oesophagogastric anastomosis. ANZ J Surg 2008;78:784–790.
8. Lamb PJ, Griffin SM, Chandrashekar MV, et al.: Prospective study of routine contrast radiology after total gastrectomy. Br J Surg 2004;91:1015–1019.
9. Tirnaksiz MB, Deschamps C, Allen MS, et al.: Effectiveness of screening aqueous contrast swallow in detecting clinically significant anastomotic leaks after esophagectomy. Eur Surg Res 2005;37:123–128.
10. Page RD, Shackcloth MJ, Russell GN, et al.: Surgical treatment of anastomotic leaks after oesophagectomy. Eur J Cardiothorac Surg 2005;27:337–343.
11. Badillo AT, Sarani B, Evans SR: Optimizing the use of blood cultures in the febrile postoperative patient. J Am Coll Surg 2002; 194:477–487.
12. Levy MM, Fink MP, Marshall JC, et al.: 2001 SCCM/ESICM/ ACCP/ATS/SIS International Sepsis Definitions Conference. Intensive Care Med 2003;29:530–538.
13. Griffin SM, Lamb PJ, Dresner SM, et al.: Diagnosis and management of a mediastinal leak following radical oesophagectomy. Br J Surg 2001;88:1346–1351.
14. Hogan BA, Winter DC, Broe D, et al.: Prospective trial comparing contrast swallow, computed tomography and endoscopy to identify anastomotic leak following oesophagogastric surgery. Surg Endosc 2008;22:767–771.
15. Upponi S, Ganeshan A, D'Costa H, et al.: Radiological detection of post-oesophagectomy anastomotic leak—A comparison between multidetector CT and fluoroscopy. Br J Radiol 2008; 81:545–548.
16. Griffin SM, Lamb PJ, Dresner SM, et al.: Diagnosis and management of a mediastinal leak following radical oesophagectomy. Br J Surg 2001;88:1346–1351.
17. Humphrey SP, Williamson RT: A review of saliva: Normal composition, flow, and function. J Prosthet Dent 2001;85:162–169.